

## REMARKS

### Specification

The specification is amended as suggested by the Examiner.

### Claim Rejections Under 35 U.S.C. §§ 112, first paragraph

Claim 16 is rejected as allegedly not enabled for deposit issues.

L19 is known in the art as is confirmed by Viti cited in the rejection, which reference teaches L19. According to 37 CFR § 1.802(b) “biological material need not be deposited, *inter alia*, if it is known and readily available to the public.” Thus, there is no requirement under the rules for applicants to provide a deposit of L19.

Additionally, Viti teaches on page 347, in the first paragraph of the section headed “Materials and Methods,” that L19 corresponds to “European Molecular Biology Laboratory accession no. AJ006113.”

With regard to the description of the cyanine dyes according to formula II in original claim 5 and in the specification, “Y” was not literally defined. In this regard, WO 96/17628 was identified in the specification on page 9, lines 6–9. The Office Action alleges that under the guidance of the MPEP, particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found. Applicants do specifically point particular attention to what portion is relevant from the WO reference. That is, applicants explicitly indicate that the “polymethine dyes, such as dicarbocyanine, tricarbo-cyanine, merocyanine and oxonol dyes (WO 96/17628)” of this reference are what is taught. This incorporated by reference all of the cited material, now explicitly added on page 9. From there, the non-new-matter definition of “Y” per the claims of this application is clearly supported. The incorporation of this information into the present application is thus supported by *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 54 USPQ2d 1673 (Fed. Cir. 2000) and is not at odds with the MPEP.

The incorporation by reference is made from Licha, US 6,083,485, which is a national phase of WO 96/17628, and thus has the same specification as WO ‘628. (If the Examiner would like a copy of the translation of WO ‘628 filed during the prosecution of Licha, please let applicants know and such will be provided.) From Licha, incorporated are cyanine dyes and merocyanine dyes. There were no specific oxonol dyes therein. Licha teaches cyanine dyes of formulae IIa and V in each of which formulae X and Y are at corresponding positions

when compared to the compounds of the present application. In each case, the definitions of X and Y are given together. The incorporation of these formulas makes explicit that the definitions of X and Y are the same (although independently from each other.)

The material being inserted is the material previously incorporated by reference and contains no new matter.

Therefore, the incorporation of the definition of Y is not new matter.

Additionally, applicants explicitly state now in the specification that WO 96/17628 is “incorporated by reference.” See 37 CFR § 1.57(g).

Claims 26 and 31 are amended to further clarify that the visualization is performed during surgery.

**Claim Rejections Under 35 U.S.C. §§ 112, second paragraph**

Claims 23, 25-28, and 30-33 are amended to explicitly recite the visualization step in the body of these claims.

Claims 26 and 31 as mentioned above are amended to further clarify that the visualization is performed during surgery.

**Claim Rejections Under 35 U.S.C. § 103**

The claims are rejected as allegedly obvious over Neri, in view of Viti, applicants’ alleged admission in the specification, and Licha.

The Office Action alleges that one of ordinary skill in the art would have found it obvious to combine the teachings of Neri and Licha “with the expected benefit that the conjugate ‘accumulates in the edge areas of the cell tissue of a focus of disease’ making the edge area of the focus of disease optically detectable.” (Emphasis added.) There is no support or basis for this allegation. Why would one of ordinary skill in the art “expect” the benefit that the conjugate accumulates in the edge areas of cell tissue of a focus of disease in a manner that permits their optical detection? Nothing in any of the cited references teaches or suggests the same to any extent. Additionally, no rationale for such an expectation is provided by the Office Action. A bare allegation without more is insufficient to establish obviousness.

Viti teaches, which is all that is alleged about this document, that L19 selectively targets newly formed blood vessels and that it has good binding affinity. Nevertheless, the Office Action alleges that since the Viti reference is using the same antibody as applicant (see

dependent claim 16), it would localize in the same place, i.e., the edge area. The claims herein however are directed not to L19, but to a conjugate of L19 and a dye as recited in the claims.

The Office Action has not established that the claimed entity, the conjugate of the claims comprising the antibody and the dye, would be expected by one of ordinary skill in the art to localize at edge areas of a focus of a disease in a manner which would allow for optical detection as claimed herein. Thus, there is no motivation to make the claimed conjugate over all other possible conjugates. None of the cited documents, alone or in any combination, leads one of ordinary skill in this art to the subject matter of the present claims.

Neither Neri or Viti teaches or suggests that a combination entity of the antibody with dyes disclosed in Licha should be formed for any reason, let alone would be useful for imaging edge areas of a focus of a disease. Licha is completely silent about the usefulness of the disclosed dyes in imaging such edge areas. Thus, there is no motivation for one of ordinary skill in the art to combine the teachings of the three references to arrive at the claimed invention on any basis whatsoever, let alone based on any expectation of the ability to optically detect edge areas of the focus of a disease such as cancer.

*In re Jones*, 958 F.2d 347 (Fed. Cir. 1992) fully supports these arguments. In *Jones*, a certain salt comprised a cation and an anion. It was known in the field that the heterocyclic anion was the basis for the herbicidal activity of the salt. It was further known that the cation could be any quaternary ammonium cation. All would work because only the anion was the basis for the activity. Nevertheless, although the particular cation in the salt claimed was conventional per se, there was still no obviousness because nothing in the prior art suggested that, among all the known operable cations, the particular one at issue should be selected. Similarly here, even if it is alleged that Neri had made clear to skilled workers that any fluorescent dye could be employed in its particular antibody conjugates including those of Licha or Viti (not admitted), more is needed to provide sufficient motivation to make the particular combination claimed. But there is nothing more of record than such alleged, mere operability offered by the Examiner as a basis for the motivation to combine the references. Under *Jones*, this basis is clearly insufficient. Thus, the rejection must be withdrawn.

In view of the above, favorable reconsideration is courteously requested. If there are any remaining issues which can be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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